

| Type | L # | Hits | Search Text | DBs   | Time Stamp                         | Comments         | Error Definiti on |
|------|-----|------|-------------|---|------------------------------------|------------------|-------------------|
| 1    | BRS | L1   | 2           | "2002000481"  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:15 | 0                 |
| 2    | BRS | L2   | 2           | "20020172661"   | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:16 | 0                 |
| 3    | BRS | L3   | 2           | 5977057 .pn.  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:33 | 0                 |
| 4    | BRS | L4   | 8           | (pharmaceutical or therapeutic\$2) adj composition  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:34 | 0                 |
| 5    | BRS | L5   | 1772        | succinate same buffer   | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:35 | 0                 |
| 6    | BRS | L6   | 125         | ((pharmaceutical or therapeutic\$2) adj composition) same (succinate same buffer)         | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:35 | 0                 |
| 7    | BRS | L7   | 12          | ((pharmaceutical or therapeutic\$2) adj composition) same (succinate same buffer) same mM | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:36 | 0                 |
| 8    | BRS | L8   | 46          | (succinate same buffer) same composition same mM  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:36 | 0                 |

| Type | L # | Hits     | Search Text  | DBs                                | Time Stamp       | Comments | Error Definiti on |
|------|-----|----------|--|------------------------------------|------------------|----------|-------------------|
| 9    | BRS | L9 2     | (succinate same buffer) same ((human adj insulin-like adj growth adj factor adj ((pharmaceutical or therapeutic\$2) adj composition) ) or IGF-1) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:37 |          | 0                 |
| 10   | BRS | L10 2186 | (human adj insulin-like adj growth adj factor adj 1) or IGF-1  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:38 |          | 0                 |
| 11   | BRS | L11 0    | 6 same 10  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:39 |          | 0                 |
| 12   | BRS | L12 0    | 8 same 10  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:39 |          | 0                 |
| 13   | BRS | L13 12   | shirley adj bret.in.   | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:55 |          | 0                 |
| 14   | BRS | L14 18   | hora adj maninder.in.  | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:55 |          | 0                 |
| 15   | BRS | L15 2    | ((shirley adj bret.in.) or (hora adj maninder.in.)) and (7 or 8)   | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/03/16 15:56 |          | 0                 |

> d his

(FILE 'HOME' ENTERED AT 16:01:17 ON 16 MAR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'  
ENTERED AT

16:01:41 ON 16 MAR 2003

L1 24950 S (PHARMACEUTIC? OR THERAPEUTIC?) (W) COMPOSITION  
L2 2100 S SUCCINATE (P) BUFFER  
L3 625 S (SUCCINIC ACID) (P) BUFFER  
L4 2617 S L2 OR L3  
L5 4 S L1 (P) L4  
L6 4 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)  
L7 135 S COMPOSITION (P) L4  
L8 92 DUPLICATE REMOVE L7 (43 DUPLICATES REMOVED)  
L9 8 S L8 (P) MM  
L10 8 S L9 NOT L6  
L11 20744 S (HUMAN INSULIN-LIKE GROWTH FACTOR 1) OR (IGF-1)  
L12 0 S L11 (P) (L5 OR L9)

=> log y

FILE 'HOME' ENTERED AT 16:01:17 ON 16 MAR 2003

=> file medline caplus biosis embase scisearch agricola  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
SESSION  
FULL ESTIMATED COST ENTRY 0.21 0.21

FILE 'MEDLINE' ENTERED AT 16:01:41 ON 16 MAR 2003

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FILE 'AGRICOLA' ENTERED AT 16:01:41 ON 16 MAR 2003

=> s (pharmaceutic? or therapeutic?) (w) composition  
L1 24950 (PHARMACEUTIC? OR THERAPEUTIC?) (W) COMPOSITION

=> s succinate (p) buffer  
L2 2100 SUCCINATE (P) BUFFER

=> s (succinic acid) (p) buffer  
L3 625 (SUCCINIC ACID) (P) BUFFER

=> s l2 or l3  
L4 2617 L2 OR L3

=> s l1 (p) l4  
L5 4 L1 (P) L4

=> duplicate remove 15  
PROCESSING COMPLETED FOR L5  
L6 4 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)

=> d 16 1-4 ibib abs

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2002:256088 CAPLUS  
DOCUMENT NUMBER: 136:299709  
TITLE: Tocol-based compositions containing amiodarone  
INVENTOR(S): Lambert, Karel J.; Kessler, Dean R.; Nienstedt, Andrew  
M.; Hartgraves, Greg A.; Constantinides, Panayiotis P.  
PATENT ASSIGNEE(S): Sonus Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 21 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2002026324 | A2   | 20020404 | WO 2001-US30320 | 20010927 |
| WO 2002026324 | A3   | 20020704 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG

AU 2001094826 A5 20020408 AU 2001-94826 20010927

PRIORITY APPLN. INFO.: US 2000-235865P P 20000927

WO 2001-US30320 W 20010927

AB \*\*\*Pharmaceutical\*\*\* \*\*\*compns\*\*\* comprising amiodarone or one of its prodrugs or analogs and one or more tocols are disclosed. An emulsion contained amiodarone 0.6, d,1-.alpha.-tocopherol 1.0, tocopherol polyethylene glycol \*\*\*succinate\*\*\* 1.0, Poloxamer P-407 0.5, PEG-400 g, and \*\*\*buffer\*\*\* q.s. 50 mL. Stability of the formulations was studied.

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:121156 CAPLUS

DOCUMENT NUMBER: 124:156044

TITLE: Pharmaceutical compositions containing hGH.

INVENTOR(S): Samaritani, Fabrizio

PATENT ASSIGNEE(S): Applied Research Systems, Neth.

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 9535116  | A1   | 19951228 | WO 1994-IT86    | 19940617 |
| W: JP, US   |      |          |                 |          |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |          |
| EP 804223   | A1   | 19971105 | EP 1994-920573  | 19940617 |
| EP 804223   | B1   | 19990922 |                 |          |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE |      |          |                 |          |
| JP 10504531   | T2   | 19980506 | JP 1994-501903  | 19940617 |
| AT 184798   | E    | 19991015 | AT 1994-920573  | 19940617 |
| ES 2139081  | T3   | 20000201 | ES 1994-920573  | 19940617 |
| US 5898030  | A    | 19990427 | US 1996-750684  | 19961217 |
| PRIORITY APPLN. INFO.:  |      |          | EP 1994-920573  | 19940617 |
|   |      |          | WO 1994-IT86    | 19940617 |

AB Pharmaceutical compns. contg. hGH were stabilized by saccharose. The formulation is particularly suitable for stabilizing a lyophilizate of recombinant hGH.

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:532058 CAPLUS

DOCUMENT NUMBER: 122:274053

TITLE: Process and apparatus for manufacturing of a pharmaceutical composition containing prednisolone sodium succinate, suitable for parenteral dosing

INVENTOR(S): Mago Karacsony, Erzsebet; Ambrus, Gabor; Balogh, Tibor; Danitz, Bela; Toldy, Lajos; Makk, Nandor; Tegdes, Aniko; Kovacs, Klara Maria; Bidlo, Gaborne; et al.

PATENT ASSIGNEE(S): Gyogyszerkutato Intezet, Hung.

SOURCE: Hung. Teljes, 14 pp.

CODEN: HUXXBU

DOCUMENT TYPE: Patent

LANGUAGE: Hungarian

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| HU 66012   | A2   | 19940829 | HU 1992-4081    | 19921222 |
| HU 212306  | B    | 19960528 |                 |          |

PRIORITY APPLN. INFO.: HU 1992-4081 19921222

AB The process involves mixing prednisolone hemisuccinate and NaOH, sterile filtering of the resultant prednisolone sodium succinate soln., filling it into ampuls, lyophilizing it, and closing the ampuls under an inert gas atm. Thus, powd. prednisolone hemisuccinate with a particle size  $\text{ltoreq.} 200 \text{ .mu.m}$  is dispersed in an aq. soln. contg.  $(9.5.+-0.2):(0.5.+-$

.0.2) wt.:wt. Na2HPO4 and NaH2PO4 as buffer substances. The dispersion is cooled to 5-15.degree., preferably to 5-10.degree.. Then 80-95%, of the stoichiometrically necessary 0.3-1.0% wt.:vol. NaOH soln. is added in portions during intensive stirring of the reaction medium and stirring is continued until the complete dissoln. of prednisolone hemisuccinate. A stainless steel reactor for carrying out the process is also claimed. In contrast to former processes this process gives only trace amts. of hydrolysis products at most.

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1990:62635 CAPLUS

DOCUMENT NUMBER: 112:62635

TITLE: Stabilized injection solutions containing nonlyophilized gamma-interferons

INVENTOR(S): Hwang-Felgner, Jiin Yu; Jones, Richard E.; Maher, James F.

PATENT ASSIGNEE(S): Genentech, Inc., USA

SOURCE: PCT Int. Appl., 15 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                    | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 8904177                                    | A1   | 19890518 | WO 1988-US3883  | 19881101 |
| W: AU, DK, FI, HU, JP, KR, NO                 |      |          |                 |          |
| RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE    |      |          |                 |          |
| IL 88233                                      | A1   | 19930818 | IL 1988-88233   | 19881030 |
| AU 8827245                                    | A1   | 19890601 | AU 1988-27245   | 19881101 |
| AU 621327                                     | B2   | 19920312 |                 |          |
| EP 386106                                     | A1   | 19900912 | EP 1988-910211  | 19881101 |
| EP 386106                                     | B1   | 19940302 |                 |          |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE |      |          |                 |          |
| JP 03500882                                   | T2   | 19910228 | JP 1988-509401  | 19881101 |
| JP 2732877                                    | B2   | 19980330 |                 |          |
| AT 102048                                     | E    | 19940315 | AT 1988-910211  | 19881101 |
| ZA 8808249                                    | A    | 19900725 | ZA 1988-8249    | 19881103 |
| DD 289470                                     | A5   | 19910502 | DD 1988-321429  | 19881103 |
| CA 1335176                                    | A1   | 19950411 | CA 1988-582102  | 19881103 |
| US 5151265                                    | A    | 19920929 | US 1990-514392  | 19900425 |
| PRIORITY APPLN. INFO.:                        |      |          | US 1987-116434  | 19871103 |
|   |      |          | EP 1988-910211  | 19881101 |
|   |      |          | WO 1988-US3883  | 19881101 |

AB A liq. \*\*\*pharmaceutical\*\*\* \*\*\*comprn\*\*\* . comprises an effective amt. of nonlyophilized .gamma.-interferon. The compn. further includes a \*\*\*buffer\*\*\* capable of maintaining the pH within 4-6, polyhydric sugar alcs. as stabilizer, and a nonionic detergent. The relative shelf-life for the liq. contg. 2 mg/mL .gamma.-interferon, mannitol, and \*\*\*succinate\*\*\* \*\*\*buffer\*\*\* was 10 days as compared to 1 day for the lyophilized formulation.

=> d his

(FILE 'HOME' ENTERED AT 16:01:17 ON 16 MAR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 16:01:41 ON 16 MAR 2003

|    |   |
|----|---|
| L1 | 24950 S (PHARMACEUTIC? OR THERAPEUTIC?) (W) COMPOSITION |
| L2 | 2100 S SUCCINATE (P) BUFFER                             |
| L3 | 625 S (SUCCINIC ACID) (P) BUFFER                        |
| L4 | 2617 S L2 OR L3   |
| L5 | 4 S L1 (P) L4   |
| L6 | 4 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)            |

=> s composition (p) l4

L7 135 COMPOSITION (P) L4

=> duplicate remove 17

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L7

L8 92 DUPLICATE REMOVE L7 (43 DUPLICATES REMOVED)

=> s 18 (p) mM

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L49 (P) MM'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L55 (P) MM'

L9 8 L8 (P) MM

=> s 19 not 16

L10 8 L9 NOT L6

=> d 110 1-8 ibib abs

L10 ANSWER 1 OF 8 MEDLINE

ACCESSION NUMBER: 88307898 MEDLINE

DOCUMENT NUMBER: 88307898 PubMed ID: 2457334

TITLE: Separation of cell organelles in density gradients based on  
their permeability characteristics.

AUTHOR: Gasser K W; DiDomenico J; Hopfer U

CORPORATE SOURCE: Department of Physiology and Biophysics, Case Western  
Reserve University, Cleveland, Ohio 44106.

CONTRACT NUMBER: AM 25170 (NIADDK)

DK 27651 (NIDDK)

HL 07415 (NHLBI)

SOURCE: ANALYTICAL BIOCHEMISTRY, (1988 May 15) 171 (1) 41-6.

Journal code: 0370535. ISSN: 0003-2697.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198809

ENTRY DATE: Entered STN: 19900308

Last Updated on STN: 19970203

Entered Medline: 19880915

AB The buoyant density of intracellular organelles is dependent in part on the nature of the \*\*\*buffer\*\*\* \*\*\*composition\*\*\* of the density gradient and the permeability characteristics of the organelle membrane to the constituents of this \*\*\*buffer\*\*\*. Therefore, knowledge of the transport properties of different organelles allows the design of density gradients useful for their purification. We have used this approach to significantly decrease mitochondrial contamination of pancreatic zymogen granules in a one-step purification procedure on a 40% Percoll density gradient. These gradients, prepared with isoosmotic sucrose, yield a narrow band of zymogen granules and mitochondria. However, by substitution of sucrose with salts to which mitochondria but not zymogen granules are permeable, the densities of mitochondria are altered to give a significant separation. For example, the incorporation of 100 \*\*\*mM\*\*\* sodium \*\*\*succinate\*\*\* in the Percoll gradient can produce a 70% reduction in mitochondrial contamination. The increased ionic strength has an additional beneficial effect on zymogen granule yield by 5-10%. The recognition and utilization of transport pathways in organelle membranes is the principal feature of this technique and should prove to be widely applicable to other isolation procedures.

L10 ANSWER 2 OF 8 MEDLINE

ACCESSION NUMBER: 83238332 MEDLINE

DOCUMENT NUMBER: 83238332 PubMed ID: 6305947

TITLE: The regulation of extramitochondrial steady state free Ca<sup>2+</sup> concentration by rat insulinoma mitochondria.

AUTHOR: Prentki M; Janjic D; Wollheim C B

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1983 Jun 25) 258 (12)  
7597-602.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198308

ENTRY DATE: Entered STN: 19900319

AB For the study of  $\text{Ca}^{2+}$  handling by mitochondria of an insulin secretory tissue, a method for the isolation of functionally intact insulinoma mitochondria is described. The mitochondria had a respiratory control ratio of  $6.3 \pm 0.3$  with \*\*\*succinate\*\*\* as a substrate. The regulation of extramitochondrial  $[\text{Ca}^{2+}]_o$  concentration by suspensions of insulinoma mitochondria was studied using  $\text{Ca}^{2+}$ -selective minielectrodes. The mitochondria were found to maintain an ambient free  $\text{Ca}^{2+}$  concentration of about 0.3 and 0.9 microM in the absence or presence of  $\text{Mg}^{2+}$  (1 \*\*\*mM\*\*\*), respectively. The addition of  $\text{Na}^+$  resulted in a dose-dependent (half-maximal 4 \*\*\*mM\*\*\*  $\text{Na}^+$ ) increase in steady state  $[\text{Ca}^{2+}]_o$ .  $\text{Na}^+$  accelerated the ruthenium red-induced  $\text{Ca}^{2+}$  efflux, suggesting the existence of a  $\text{Ca}^{2+}/2\text{Na}^+$  antiporter, as described in mitochondria of excitable tissues. Experiments were performed to study the effects of various agents on the steady state extramitochondrial free  $\text{Ca}^{2+}$ . cAMP, 3-isobutyl-1-methylxanthine, and NADH were found to have no effect, whereas phosphoenolpyruvate induced a net  $\text{Ca}^{2+}$  efflux, the kinetic of which suggests deleterious effects on mitochondrial functions. A small decrease in pH (0.1 unit) of the incubation \*\*\*buffer\*\*\* resulted in an increase of the extramitochondrial  $\text{Ca}^{2+}$  steady state that was reversible upon restoration of the pH to its initial value. In conclusion, insulinoma mitochondria were able to maintain an extramitochondrial  $[\text{Ca}^{2+}]_o$  steady state in the submicromolar range that was markedly influenced by the ionic \*\*\*composition\*\*\* of the incubation medium. Thus, mitochondria may play a role in the regulation of cellular calcium homeostasis and insulin release.

L10 ANSWER 3 OF 8 MEDLINE

ACCESSION NUMBER: 83230736 MEDLINE

DOCUMENT NUMBER: 83230736 PubMed ID: 6860312

TITLE: Photosynthetic electron transport in thylakoid preparations from two marine red algae (Rhodophyta).

AUTHOR: Stewart A C; Larkum A W

SOURCE: BIOCHEMICAL JOURNAL, (1983 Feb 15) 210 (2) 583-9.

Journal code: 2984726R. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198307

ENTRY DATE: Entered STN: 19900319

Last Updated on STN: 19900319

Entered Medline: 19830729

AB Thylakoid membrane preparations active in photosynthetic electron transport have been obtained from two marine red algae, *Griffithsia monilis* and *Anotrichium tenue*. High concentrations (0.5-1.0 M) of salts such as phosphate, citrate, \*\*\*succinate\*\*\* and tartrate stabilized functional binding of phycobilisomes to the membrane and also stabilized Photosystem II-catalysed electron-transport activity. High concentrations (1.0 M) of chloride and nitrate, or 30 \*\*\*mM\*\*\* -Tricine/NaOH \*\*\*buffer\*\*\* (pH 7.2) in the absence of salts, detached phycobilisomes and inhibited electron transport through Photosystem II. The  $\text{O}_2$ -evolving system was identified as the electron-transport chain component that was inhibited under these conditions. Washing membranes with \*\*\*buffers\*\*\* containing 1.0-1.5 M-sorbitol and 5-50 \*\*\*mM\*\*\* concentrations of various salts removed the outer part of the phycobilisome but retained 30-70% of the allophycocyanin 'core' of the phycobilisome. These preparations were 30-70% active in  $\text{O}_2$  evolution compared with unwashed membranes. In the sensitivity of their  $\text{O}_2$ -evolving apparatus to the \*\*\*composition\*\*\* of the medium in vitro, the red algae resembled blue-green algae and differed from other eukaryotic algae and higher plants. It is suggested that an environment of structured water may be essential for the functional integrity of Photosystem II in biliprotein-containing algae.

L10 ANSWER 4 OF 8 MEDLINE

ACCESSION NUMBER: 76260253 MEDLINE

DOCUMENT NUMBER: 76260253 PubMed ID: 783158

TITLE: Effect of cations and anions on the steady state kinetics of energy-dependent  $\text{Ca}^{2+}$  transport in rat liver mitochondria.

AUTHOR: Hutson S M; Pfeiffer D R; Lardy H A  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1976 Sep 10) (17) 5251-8.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 197611  
 ENTRY DATE: Entered STN: 19900313  
 Last Updated on STN: 19970203  
 Entered Medline: 19761101

AB The divalent cation ionophore A23187 has been used to investigate the kinetics of energy-dependent  $Ca^{2+}$  uptake by rat liver mitochondria under steady state conditions. During A23187-induced cyclic  $Ca^{2+}$  flux, the free  $Ca^{2+}$  concentration is adjusted using [ethylenebis(oxyethylenenitrilo)]tetraacetic acid (EGTA) \*\*\*buffers\*\*\*. The rate of  $Ca^{2+}$  transport, which is inferred from the rate of \*\*\*succinate\*\*\* oxidation, is a function of the free  $Ca^{2+}$  concentration in the medium. The kinetics are sigmoidal with the free  $Ca^{2+}$  concentration at half-maximal respiratory stimulation ( $K_{0.5}$ ) equal to  $3.1 +/- 0.4 \mu M$  at 25 degrees. The maximal  $Ca^{2+}$ -stimulated respiratory rate ( $V_{max}$ ) is a function of the ionic \*\*\*composition\*\*\* of the medium. Magnesium and  $Mg^{2+}$  plus phosphate produced a parallel stimulation of the maximal respiration rate whether activated by  $Ca^{2+}$  uptake or by the uncoupler carbonyl cyanide-p-trifluoromethoxyphenylhydrazone (FCCP). In the absence of A23187,  $Ca:O$  ratios of 4.0 were obtained under most experimental conditions. Magnesium is a potent competitive-like inhibitor, increasing the  $K_{0.5}$  for  $Ca^{2+}$  to  $30.0 \mu M$  at  $2.0 \text{ mM}$   $MgCl_2$ . Magnesium dramatically decreases the apparent affinity for  $Ca^{2+}$  but does not appear to alter the kinetic mechanism. In contrast, the alkali metal cations are weak inhibitors, at most doubling the  $K_{0.5}$  for  $Ca^{2+}$ ; however, they antagonized  $Mg^{2+}$  inhibition with an order of effectiveness  $Li^+$  greater than or equal to  $Na^+$  greater than  $K^+$  greater than  $Rb^+ = Cs^+$ . Phosphate and acetate increased the  $V_{max}$  slightly without altering the  $K_{0.5}$  for  $Ca^{2+}$ . Phosphate did not influence the inhibitory effects of  $Mg^{2+}$  or  $Mg^{2+}$  plus  $K^+$ . This study suggests that during steady state conditions, the maximal rate of  $Ca^{2+}$  accumulation is primarily electron transport-limited. The results are also discussed in terms of a possible physiological role for  $Mg^{2+}$  and  $K^+$  in the intracellular regulation of energy-dependent mitochondrial  $Ca^{2+}$  transport in liver.

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1994:79106 CAPLUS  
 DOCUMENT NUMBER: 120:79106  
 TITLE: Manufacture of transparent moldings with hard surface  
 INVENTOR(S): Uenishi, Michiharu; Nagai, Shoichi; Takei, Masatoshi;  
 Kobayashi, Yukio; Akagi, Juji  
 PATENT ASSIGNEE(S): Mitsubishi Rayon Co, Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------|------|----------|-----------------|----------|
| JP 05228431 | A2   | 19930907 | JP 1992-32341   | 19920219 |

PRIORITY APPLN. INFO.: JP 1992-32341 19920219

AB Title moldings, useful for building, automotive, and optical applications (no data), are manufd. by irradiating moldings bearing on surface a layer of polymers derived from monomers contg. .gtoreq.2 (meth)acryloyl groups and other monomers with UV light of wavelengths .ltoreq.300 nm, treating the irradiated moldings with alkali to generate .gtoreq.0.02 .mu.mol acidic groups/cm<sup>2</sup> on the surface, coating the surface with hydrolytic polycondensation products of  $XaSi(OY)4-a$  (X = epoxy-contg. functional group; Y = hydrocarbyl; a = 1-3) and/or  $SiR1bR2c(OR3)d$  [R1, R2 = (ether or ester linkage-contg.) hydrocarbyl; R3 = H, hydrocarbyl; b, c = 0-3; d = 4 - b - c = 1-4; b + c = 1-3], and contacting the polycondensation products with a high-temp. fluid at .gtoreq.500.degree.. Thus, a 2 \*\*\*mm\*\*\*-thick PMMA sheet was dip-coated with a soln. contg. dipentaerythritol

hexaacrylate 10, equimolar \*\*\*succinic\*\*\* \*\*\*acid\*\*\*  
 -trimethylolethane-acrylic acid condensation product 20,  
 tetrahydrofurfuryl acrylate 5, Darocur 1173 1.2, isopropanol 34, and  
 toluene 20% and irradiated with UV (365 nm, 840 mJ/cm<sup>2</sup>) at 35.degree. to  
 form a 3.5 .mu.m-thick film with pencil hardness 5H, which was further  
 UV-irradiated (254 nm, 1300 mJ/cm<sup>2</sup>) and immersed in 20% aq. NaOH to  
 generate 0.05 .mu.mol acidic groups/cm<sup>2</sup>. The sheet was dip-coated with a  
 \*\*\*compn\*\*\* . of .gamma.-glycidoxypropyltrimethoxysilane 100.4,  
 isopropanol 278.3, tetraethoxysilane 40.0, 0.2 N AcOH/NaOAc (pH 5)  
 \*\*\*buffer\*\*\*, and Mg perchlorate 2.0 parts, held at 100.degree. for 3 h, then brought into contact with a natural gas flame of 900.degree. 20 times for .apprx.0.2 s each time. The cured coat showed good Taber abrasion resistance, cross-cut adhesion 100/100 initially and 100/100 after 20-h immersion in H<sub>2</sub>O at 80.degree., and smooth crack-free surface before and after the hot water immersion.

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:639540 CAPLUS

DOCUMENT NUMBER: 111:239540

TITLE: Liposomes containing hydrophilic drugs and a process for manufacture them

INVENTOR(S): Profitt, Richard Thomas; Adler-Moore, Jill; Chiang, Su-Ming

PATENT ASSIGNEE(S): Vestar, Inc., USA

SOURCE: Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| EP 317120   | A1   | 19890524 | EP 1988-310278  | 19881101    |
| EP 317120   | B1   | 19910828 |                 |             |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |             |
| AU 8824161  | A1   | 19890518 | AU 1988-24161   | 19881024    |
| AU 598958   | B2   | 19900705 |                 |             |
| AT 66598  | E    | 19910915 | AT 1988-310278  | 19881101    |
| ES 2029330  | T3   | 19920801 | ES 1988-310278  | 19881101    |
| KR 9707187  | B1   | 19970507 | KR 1988-14547   | 19881105    |
| NO 8804989  | A    | 19890516 | NO 1988-4989    | 19881109    |
| NO 178484   | B    | 19960102 |                 |             |
| NO 178484   | C    | 19960410 |                 |             |
| JP 01160915   | A2   | 19890623 | JP 1988-284828  | 19881110    |
| JP 2958774  | B2   | 19991006 |                 |             |
| CA 1339008  | A1   | 19970325 | CA 1988-582730  | 19881110    |
| DK 8806293  | A    | 19890513 | DK 1988-6293    | 19881111    |
| US 5965156  | A    | 19991012 | US 1995-469251  | 19950606    |
| PRIORITY APPLN. INFO.:                                |      |          | US 1987-119518  | A 19871112  |
|   |      |          | EP 1988-310278  | A 19881101  |
|   |      |          | US 1990-600154  | A1 19901019 |

AB A novel liposome \*\*\*compn\*\*\* . and a method for solubilizing amphiphilic drugs in a small amt. of org. solvent for use in improved liposomes are described. A phosphatidylglycerol is acidified and the amphiphilic drugs suspended in an org. solvent are added to solubilize the drugs. Distearoylphosphatidylglycerol Na soln. dissolved in CHCl<sub>3</sub>-MeOH mixt. (1:1) was acidified with HCl and then mixed with amphotericin B (I) soln. dissolved in the same solvent. Hydrogenated egg phosphatidylcholine soln. and cholesterol soln. dissolved in the same solvent were then mixed with the mixt. The pH was adjusted to 4.5 by addn. of 2.5 N NaOH. The molar ratio of I, distearoylphosphatidylglycerol, hydrogenated egg phosphatidylcholine, and cholesterol in the soln. was 0.4, 0.4, 2.0, and 1.0 resp. The lipid soln. was spray-dried to give a powder, which was hydrated with 9% lactose-contg. 10 \*\*\*mM\*\*\* \*\*\*succinate\*\*\*

\*\*\*buffer\*\*\* (pH 5.62) and sonicated to give liposomes. Mice were i.v. inoculated with Candida albicans and 3 days post-infection, mice were treated with a single dose of either free I or liposomal I. There was no dose level of free I which produced any survivors at 29 days post-infection; however, all animals treated with 10 or 15 mg/kg of liposomal I were still alive 42 days post-infection.

ACCESSION NUMBER: 1989:5807 CAPLUS

DOCUMENT NUMBER: 111:180738

TITLE: Sustained-release pharmaceuticals containing a soluble metoprolol salt and a dihydropyridine in a gel-forming matrix

INVENTOR(S): Ragnarsson, Gert Anders; Silfverstrand, Kajsa  
Margareta; Sjoegren, John Albert

PATENT ASSIGNEE(S): Aktiebolag Haessle, Swed.

SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

| PATENT NO.  | KIND  | DATE     | APPLICATION NO. | DATE     |
|-------------|---|----------|-----------------|----------|
| EP 311582   | A1  | 19890412 | EP 1988-850319  | 19880922 |
| EP 311582   | B1  | 19930113 |                 |          |
|             | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |          |                 |          |
| AU 8822374  | A1  | 19890413 | AU 1988-22374   | 19880916 |
| AU 615211   | B2  | 19910926 |                 |          |
| AT 84412    | E   | 19930115 | AT 1988-850319  | 19880922 |
| ES 2053815  | T3  | 19940801 | ES 1988-850319  | 19880922 |
| NO 8804269  | A   | 19890410 | NO 1988-4269    | 19880927 |
| NO 177375   | B   | 19950529 |                 |          |
| NO 177375   | C   | 19950906 |                 |          |
| US 4942040  | A   | 19900717 | US 1988-250945  | 19880929 |
| IL 87922    | A1  | 19930708 | IL 1988-87922   | 19881005 |
| DK 8805586  | A   | 19890409 | DK 1988-5586    | 19881006 |
| FI 8804636  | A   | 19890409 | FI 1988-4636    | 19881007 |
| FI 92903    | B   | 19941014 |                 |          |
| FI 92903    | C   | 19950125 |                 |          |
| JP 01128917 | A2  | 19890522 | JP 1988-252209  | 19881007 |
| CA 1312286  | A1  | 19930105 | CA 1988-579566  | 19881007 |
| CN 1032490  | A   | 19890426 | CN 1988-109129  | 19881008 |
| CN 1029935  | B   | 19951011 |                 |          |

PRIORITY APPLN. INFO.: SE 1987-3881 19871008  
EP 1988-850319 19880922

AB A controlled-release pharmaceutical for once daily administration contains metoprolol and a poorly water-sol. Ca channel blocking agent of the dihydropyridine type; metoprolol is included in the form of small beads contg. as the main sol. component a salt of metoprolol coated with a water-insol. polymeric membrane. The dihydropyridine is dispersed in a nonionic solubilizer. Both, the dispersed dihydropyridine and the metoprolol-contg. beads are incorporated in a matrix forming a swelling agent when in contact with water. A mixt. contg. felodipine, Polyoxyl-40 hydrogenated castor oil (solubilizer), Polyvdon-K90, hydroxypropyl Me cellulose (swelling agent), Al silicate, lactose, and microcryst. cellulose was granulated with EtOH and dried. Metoprolol

\*\*\*succinate\*\*\* was sprayed onto cores of SiO<sub>2</sub> to form beads (0.5 \*\*\*mm\*\*\* diam.) and the beads were coated by spraying with a soln. contg. Et cellulose, hydroxypropyl Me cellulose in CH<sub>2</sub>Cl<sub>2</sub>/iso-PROH; the beads and granules were mixed, a lubricant was added and the \*\*\*compn\*\*\* . was pressed into tablets. Tablets contg. 10 mg felodipine and 95 mg metoprolol \*\*\*succinate\*\*\* each were prep'd. from a mixt. contg. felodipine 10, Polyoxyl-40 25, Polyvdon-K90 24, hydroxypropyl Mg cellulose 230, Al silicate 94, lactose 56, microcryst. cellulose 6, metoprolol \*\*\*succinate\*\*\* 95, SiO<sub>2</sub> 24, Et cellulose 32, and addl. hydroxypropyl Me cellulose 8 g. The dissoln. rate of felodipine in phosphate \*\*\*buffer\*\*\* contg. 1% Na dodecyl sulfate was 14, 64, 88, and 98% after 2, 8, 12, and 20 h, resp.; the dissoln. rater of metoprolol \*\*\*succinate\*\*\* was 5, 39, 65, and 95% after 2, 8, 12, and 20 h, resp. Suitable polymers for coating the beads are Eudragit RL, Eudragit RS, alone or in combination; Et cellulose in combination with hydroxypropyl Me cellulose or hydroxypropyl cellulose is preferred.

AUTHOR(S): colorimetry of dehydrogenase activity in shellfish using tetrazolium chloride  
Tsunoda, Kojun; Inoue, Noriko; Aoyama, Mitsuo; Hasebe, Akihisa  
CORPORATE SOURCE: Suginami Ward Inst. Public Health, Tokyo, 168, Japan  
SOURCE: Shokuhin Eiseigaku Zasshi (1986), 27(5), 487-91  
DOCUMENT TYPE: Journal  
LANGUAGE: Japanese

AB A simple colorimetry procedure for the detn. of dehydrogenase [9035-82-9] activity in shellfish was based on redn. of triphenyltetrazolium chloride (TTC) to triphenylformazan (TF). The dehydrogenase activity in shellfish muscle is low. When pH 7.4 phosphate \*\*\*buffer\*\*\* was added to the TTC reagent, dehydrogenase activity in shellfish muscle was increased markedly. The best \*\*\*compn\*\*\* of TTC reagent was 0.2% TTC-0.1% Na \*\*\*succinate\*\*\* -2.84% Na<sub>2</sub>HPO<sub>4</sub>-2.34% NaCl. A sample of shellfish muscle was sliced about 1.5 \*\*\*mm\*\*\* thick, soaked in TTC reagent, incubated at 37.degree. for 30 min, cooled, extd. with EtOH, filtered, and measured at 284 nm. It was also possible to det. dehydrogenase activity in oyster gills by using this TTC reagent.

=> d his

(FILE 'HOME' ENTERED AT 16:01:17 ON 16 MAR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 16:01:41 ON 16 MAR 2003

L1 24950 S (PHARMACEUTIC? OR THERAPEUTIC?) (W) COMPOSITION  
L2 2100 S SUCCINATE (P) BUFFER  
L3 625 S (SUCCINIC ACID) (P) BUFFER  
L4 2617 S L2 OR L3  
L5 4 S L1 (P) L4  
L6 4 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)  
L7 135 S COMPOSITION (P) L4  
L8 92 DUPLICATE REMOVE L7 (43 DUPLICATES REMOVED)  
L9 8 S L8 (P) MM  
L10 8 S L9 NOT L6

=> s (human insulin-like growth factor 1) or (igf-1)  
4 FILES SEARCHED...

L11 20744 (HUMAN INSULIN-LIKE GROWTH FACTOR 1) OR (IGF-1)

=> s l11 (p) (15 or 19)  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L73 (P)'  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L76 (P)'  
L12 0 L11 (P) (L5 OR L9)

=> d his

(FILE 'HOME' ENTERED AT 16:01:17 ON 16 MAR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 16:01:41 ON 16 MAR 2003

L1 24950 S (PHARMACEUTIC? OR THERAPEUTIC?) (W) COMPOSITION  
L2 2100 S SUCCINATE (P) BUFFER  
L3 625 S (SUCCINIC ACID) (P) BUFFER  
L4 2617 S L2 OR L3  
L5 4 S L1 (P) L4  
L6 4 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)  
L7 135 S COMPOSITION (P) L4  
L8 92 DUPLICATE REMOVE L7 (43 DUPLICATES REMOVED)  
L9 8 S L8 (P) MM  
L10 8 S L9 NOT L6  
L11 20744 S (HUMAN INSULIN-LIKE GROWTH FACTOR 1) OR (IGF-1)  
L12 0 S L11 (P) (L5 OR L9)

=> log y

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| SINCE FILE<br>ENTRY | TOTAL<br>SESSION |
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